



THE
BLADDER CANCER
COMPANY

Photocure Announces the Publication of Pre-Clinical Study Results Supporting the Anti-tumor Effect of Hexaminolevulinate with Blue Light in Bladder Cancer model

Press release – Oslo, Norway, 28 February 2022: Photocure ASA (OSE: PHO), the Bladder Cancer Company, announces the publication of new results from its exploratory research program in the journal *Biomedicine*, entitled “Antitumor Effect and Induced Immune Response Following Exposure of Hexaminolevulinate (HAL) and Blue Light in an Orthotopic Model of Rat Bladder Cancer”. These results support initial pre-clinical data on the potential anti-tumor effect of HAL, which were presented at the BLADDER 2019 congress [<https://photocure.com/news/photocure-new-data-from-hexvixr-trials-presented-at-the-bladdr-2019-congress-3457632>].

The study objective was based on the hypothesis that the positive impact on long-term outcomes in NMIBC patients who had undergone Blue Light Cystoscopy (BLC) prior to cystectomy could be caused by a direct anti-tumor effect and/or activation of the immune system indicating an additional effect of Blue Light with HAL beyond pure detection. Therefore, as an exploratory preclinical study, the authors investigated whether intravesical administration of HAL followed by a diagnostic blue-light illumination-regime, aiming to mimic the one used currently in Photodynamic Diagnosis (PDD), could have anti-tumor and/or immune modulating effects as seen with Photodynamic therapy (PDT). In addition, it was explored if co-administration of a checkpoint inhibitor would increase the susceptibility to the PD-1/PD-L1 pathway inhibition thus increasing the anti-tumor effect. Over the years, Photocure has conducted a number of experiments on “mechanisms of actions” effects of HAL, as well as to see if there potentially are similar anti-tumor and immune modulating effects of PDD with blue light as reported with PDT. For this study, rats were treated with HAL and blue light in an orthotopic model of bladder cancer, and then subjected to histopathological analysis of the bladder samples and additional assessment of immune markers. Co-administration of HAL and blue light with a checkpoint inhibitor was further evaluated in this model aiming to assess for potentiation of anti-tumor effects when combined with an immunotherapy.

Results of the study demonstrated an anti-tumor effect of HAL and blue light when aiming to mimic the dosing regimen of a photodynamic diagnostic procedure (PDD) in an orthotopic bladder cancer model in rats.

The authors conclude *"The anti-tumor effect is most probably pertaining to stimulation of the immune system as evident by tumor infiltration of CD3+ and CD8+ T-cells. These results support our hypothesis that the positive impact on patient outcomes observed in patients who had undergone BLC prior to cystectomy could be explained by systemic immune activation induced by HAL and blue light. Combination of HAL and blue light with intravesical anti-PD-L1 resulted in increased anti-tumor effects. Further studies are warranted to explore the long-term effects of HAL and blue light alone or in combination with checkpoint inhibitors which should extend to investigate any systemic (abscopal) effects. Intriguingly is also the idea that local treatment with HAL and blue light can prime an immune response with potential additional effect of checkpoint inhibitors."*

"The intriguing results from this pre-clinical study are encouraging and might explain an effect of HAL+BL beyond pure detection. The results motivate further research to evaluate the potential of HAL as a photodynamic therapy (PDT), which may be an innovative technique for treatment of non-muscle invasive bladder cancer," said Anders Neijber, Vice President, Global Medical Affairs and Clinical Development at Photocure.

Read the full article here: <https://www.mdpi.com/2227-9059/10/3/548>

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About Bladder Cancer

Bladder cancer ranks as the seventh most common cancer worldwide, with 1 720 000 prevalent cases (5-year prevalence rate)^{1a}, 573 000 new cases and more than 200 000 deaths annually in 2020.^{1b}

Approx. 75% of all bladder cancer cases occur in men.¹ It has a high recurrence rate, with an average of 61% in year one and 78% over five years.² Bladder cancer has the highest lifetime treatment costs per patient of all cancers.³

Bladder cancer is a costly, potentially progressive disease for which patients have to undergo multiple cystoscopies due to the high risk of recurrence. There is an urgent need to improve both the diagnosis and the management of bladder cancer for the benefit of patients and healthcare systems alike.

Bladder cancer is classified into two types, non-muscle invasive bladder cancer (NMIBC) and muscle-invasive bladder cancer (MIBC), depending on the depth of invasion in the bladder wall. NMIBC remains in the inner layer of cells lining the bladder. These cancers are the most common (75%) of all cases and include the subtypes Ta, carcinoma in situ (CIS), and T1 lesions. In MIBC, the cancer has grown into deeper layers of the bladder wall. These cancers, including subtypes T2, T3, and T4, are more likely to spread and are harder to treat.⁴

¹ Globocan. a) 5-year prevalence / b) incidence/mortality by population. Available at: <https://gco.iarc.fr/today>, accessed [January 2022].

² Babjuk M, et al. Eur Urol. 2019; 76(5): 639-657

³ Sievert KD et al. World J Urol 2009;27:295–300

⁴ Bladder Cancer. American Cancer Society. <https://www.cancer.org/cancer/bladder-cancer.html>

About Hexvix®/Cysview® (hexaminolevulinate HCl)

Hexvix/Cysview is a drug that preferentially accumulates in cancer cells in the bladder, making them glow bright pink during Blue Light Cystoscopy (BLC®). BLC with Hexvix/Cysview, compared to standard

white light cystoscopy alone, improves the detection of tumors and leads to more complete resection, fewer residual tumors, and better management decisions.

Cysview is the tradename in the U.S. and Canada, Hexvix is the tradename in all other markets. Photocure is commercializing Cysview/Hexvix directly in the U.S. and Europe and has strategic partnerships for the commercialization of Hexvix/Cysview in China, Chile, Australia, and New Zealand. Please refer to <https://photocure.com/partners/our-partners> for further information on our commercial partners.

About Photocure ASA

Photocure: The Bladder Cancer Company delivers transformative solutions to improve the lives of bladder cancer patients. Our unique technology, making cancer cells glow bright pink, has led to better health outcomes for patients worldwide. Photocure is headquartered in Oslo, Norway, and listed on the Oslo Stock Exchange (OSE: PHO). For more information, please visit us at www.photocure.com, www.hexvix.com, www.cysview.com

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